

Cytologic Detection of Cervical Cancer

Four Years' Experience with Routine Smear Examination in Private Practice

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BETTER CONTROL OF CERVICAL CANCER still depends primarily on earlier detection. The publication in 1943 of the well known Papanicolaou and Traut¹² monograph on vaginal smears seemed to give promise of widespread early detection. Since then, many research center^{1-3, 5-9, 13} and several cancer detection centers^{4, 10} have reported a high degree of success in early cancer detection using various modifications of the original Papanicolaou-Traut technique. Yet population screening with this method is still not generally available. Economic and technical obstacles, shortage of trained cytologists and valid fears of misuse have limited the use of this means of detection. Cervical cancer remains a disease which, more often than not, is already lethal by the time it is diagnosed. A method of control seems at hand, yet practical techniques for widespread application of this method have not been fully worked out.

The study herein reported upon was started nearly four years ago in an effort to adapt the use of Papanicolaou smears to private clinical practice and then to test the private physician's office as a cervical cancer detection center. It seemed reasonable that every physician's office where women are accustomed to go should be the most available and economical cancer detection center. Accordingly, attempt was made to devise and to test a procedure of technician screening that would be simple and convenient enough for any physician to use, economical enough to pay its own way in private practice, yet accurate enough to detect unsuspected cervical cancer in a high proportion of cases.

Last year a preliminary report was made on the early development of this program, the details of the simplified technique, and the number of unsuspected cases of cancer detected in a series of 7,530 smears.¹¹ From the preliminary study it was concluded that when adequate laboratory facilities were available the office of a physician in private practice could be a practical center for screening for cervical cancer. The system used was econom-

• Simplified Papanicolaou smear techniques appear to be adaptable to private clinical practice when experienced cytodetection laboratory facilities are available. A private physician's office seems potentially an efficient, economical and practical place for detection of cervical cancer by use of the smear technique as a routine part of examination of patients.

In a series here reported upon, examination of 11,207 cervical smears taken at the first examination of patients of all ages led to diagnosis of unsuspected malignant disease in 80 cases—in all instances at a stage when it should be easily curable. Cancer was not detected in examination of 6,060 smears taken later from women who had had a "negative" smear at the time of first examination, which seems to indicate that the first screening was reasonably accurate.

In a few cases, early cancer was detected when smears were reported as "atypical" or "suspicious." Such reports demand as careful follow-up as do "positive" reports.

There are dangers and limitations in widespread clinical application of screening by this method. Care must be observed in the development of programs for its use lest the potential benefits in early detection be outweighed by the dangers from misuse.

ically satisfactory to both physician and patient. With the simplified technique that was used, unsuspected intra-epithelial or early invasive cancer was detected in 43 women observed in private practice. In all instances the lesion was at a stage when it should be easily curable. All adult age groups were represented. It was further observed that routine smears on all women, regardless of age or complaint, produced as high a yield as occasional smears taken "when indicated by age or the appearance of the cervix."

The study has grown since that report and now includes for detailed analysis 17,267 smears from more than 11,000 private patients who are representative of the adult female population of San Diego

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County in all but the lowest economic brackets. Eight collaborating gynecologists who are members of the Gynob Clinical Group but practice individually, now routinely obtain smears of material from the cervix of all patients the first time they examine them, and all patients are urged to have smears taken annually thereafter.

The technique used has remained essentially as previously reported. Without previous preparation and without regard for recent douching, an ordinary tongue blade is used to scrape the region of the external os. Collected material is spread thinly on a slide which is dropped wet into ether and alcohol, then later sent to the laboratory. This step in a routine pelvic examination takes but a moment, but during that moment the patient is told: "This is a routine test for cancer. It applies to the cervix only. It should be repeated annually." Later, if the smear is "negative" a form note is sent from the physician's office to the patient, reporting that the smear gave no evidence of cancer of the cervix and again stressing the limits of relative protection: For the cervix only and for a year only. A charge of \$3.50 per slide brings the test within the reach of practically every patient and yet is enough to cover the laboratory cost with the present volume.

In the laboratory of the Gynob Clinical Group the smears are stained and examined by specially trained technicians, who classify them as "negative," "atypical," "highly atypical," "suspicious," or "positive." These classes correspond to Papanicolaou classes I, II, III, IV and V, but the terms were chosen because they seem to be more suggestive to clinicians receiving the reports. Slides in the last three classes are reexamined by a physician cytologist. In any case in which the slide is confirmed as highly atypical, suspicious or positive, biopsy specimens are taken from several sites or conization with a scalpel is carried out. For smear screening the authors have coined the term *cytodetection* as preferable to *cytodiagnosis*, since in all cases diagnosis is made by a certified pathologist from tissue preparations, not smears. Treatment is never started until a diagnosis has been made by biopsy.

In the interest of practical efficiency the original practice of making three slides for each patient was abandoned. At first, material was obtained by vaginal aspiration, by cervical scraping and by swab from the cervical canal. It was found, however, that an experienced technician could process about 600 slides a month and that making three slides for each patient barely affected the number of cases detected, yet reduced the technician's capacity to 200 patients per month. Also, it trebled the cost per patient. Since the principal yield in detection of unsuspected cancer comes from cytologic examination of material

from patients not previously examined, study of single slides of material scraped from the cervix in 600 cases will detect almost three times as many cancers as study of three slides from each of 200 patients. Moreover, it was observed that endometrial cancer was not consistently detected by examination of material aspirated from the vagina or swabbed from the cervical canal. Fortunately, endometrial cancer usually causes abnormal bleeding which leads to curettement and diagnosis before a lethal stage has been reached. For cervical cancer, on the other hand, it is felt that examination of smears is more accurate than random biopsy, for an early lesion often is not visible and tissue excised for biopsy may be taken from the wrong place to detect it.

Gradually, as experience has widened, series of smears beyond the first have been accumulated in a number of cases, which serves as a check on the accuracy of the original screening. Demand for "cancer detection smears" seems to be growing among women in San Diego. Other local physicians are taking smears and other laboratories are reporting on them. Since not only great benefits but also dangers, limitations and pitfalls are apparent, the authors take this opportunity to review their now widened experience and appraise the results, good and bad.

RESULTS IN A 4-YEAR PERIOD

In a period of four years, 17,267 smears of material scraped from the cervix of patients observed in private practice were examined. Of that total, 11,207 were from women who had not previously had examination of smears, and in 112 cases cancer was detected by the cytologic examination. In 80 of those cases, cancer was not suspected until the slides were examined; and in 74 of the 80 the growth was intra-epithelial, in 6 in an early invasive stage. In 25 of the detected cases, cancer was suspected on the basis of clinical observations or was known to be present at the time the smear was taken, and in all those cases in which there were clinical manifestations the growth was invasive. In seven cases the cancer was adenocarcinoma of the fundus of the uterus. The other 6,060 slides were annual repeat smears from women who had had at least one previous smear examination, and cancer was not found in any case.

In the entire series there were 26 cases in which the slides were reported as positive for cancer which was not confirmed by biopsy ("false positive") although in many of these cases basal cell hyperplasia explained the abnormal smears. In two cases there were "false negative" reports, which will be discussed later.

As has been said, all patients are urged to have a smear examination each year. In four years many

TABLE 1.—Atypical and suspicious smears—false positives and false negatives

Smear Report	Lost to Follow-Up	Neg. Biopsy (False Positive)	Leukoplakia or Dyskeratosis	Preinvasive Unrecognized	Invasive Unrecognized	Invasive Recognized
Neg. (I-II)	1	? 1
Highly atypical (III)	4	4	9	5	0
Suspicious (IV)	7	5	9	9	1	2
Positive (V)	9	7	19	60	5	23

patients had two, three or four. The fact that in 6,060 such examinations there has been no "positive" finding when the original result was "negative" seems an important confirmation of the accuracy of the initial screening. If many cancers were being missed on the first smear, certainly a few "positives" would show up in more than 6,000 repeat smears taken a year or more later. The authors are beginning to doubt that even an annual smear examination is necessary once there is "negative" finding. Perhaps the interval could safely be extended to two years or more.

A few patients who had "suspicious" or "positive" smears were not examined further by the authors, owing to their moving away from the area or switch to other physicians. Included among them were five who had "positive" smears and on whom deep cervical cauterization was carried out at the time of the original examination. Subsequent follow-up by smear and biopsy gave no evidence of cancer. Undoubtedly, unrecognized intra-epithelial cancer often is cured by ordinary cautery. Since this observation was made early in the study, the authors now rarely cauterize the cervix before a smear is reported as "negative."

In a number of cases in which smears were reported as "suspicious" or "positive," no evidence of malignant change could be found in biopsy specimens. Careful and prolonged observation is indicated in such circumstances. In 18 cases "atypical," "suspicious" and "positive" smears led to detection of basal hyperplasia or dyskeratosis (Table 1) which is thought by some investigators to be precancerous or a precursor of intra-epithelial cancer which is to develop later.

Of greatest importance in smear screening is the "false negative"—cancer missed by smear examination. In the present series this is known to have occurred in one case, and probably in another. In one of those cases the smear was reported as "slightly atypical." Curettement and conization were done on clinical indications and intra-epithelial carcinoma was diagnosed by biopsy. On review, the smear was classified as "suspicious." In the other case, six months after the patient had a "negative" smear on the first visit it was reported from another city that she had early invasive inverting cervical cancer. There were no other known instances of "false negative."

In several cases smears that were "atypical" and "suspicious" rather than "positive" led to detection of preinvasive cancer, and in one instance to detection of early invasive cancer whose presence was not previously recognized. It is now felt, therefore, that biopsy should be done when smears are reported as atypical or suspicious as well as when they are classified as positive.

In ten cases in the present series carcinoma of the fundus of the uterus was diagnosed; it was detected by smear examination in seven cases and missed by that method in three. The presence of the disease was suspected clinically in all the cases, owing to abnormal bleeding. It would appear that cervical smears alone should not be relied upon for detecting fundal carcinoma.

LIMITATIONS AND DANGERS

With increasing use of the smear technique, not only by the Gynob Clinical Group but by other physicians as well, some of the limitations and dangers of use of the method by physicians in private practice have become apparent. Women hear of the "cancer detection smear" and often request it from physicians who are not prepared. Inexperienced study of smears may result in false security and continued growth of cancer from a curable to an incurable stage. Smears must not replace biopsy for diagnosis of suspicious lesions.

In a case observed by one of the authors, adenocarcinoma was suspected clinically but the report on a smear was "negative" and inadvertently a report to that effect was sent to the patient. Thus, with false security, she did not keep an appointment for curettement and for a time could not be traced. Treatment was delayed two months.

It is known that in some instances physicians advised hysterectomy solely because of a "suspicious" smear. On the other hand, some patients who did not have cancer but who had smears reported as "suspicious" or "positive" suffered severely from cancerophobia before the ultimate diagnosis was reached.

DISCUSSION

It is difficult to estimate the number of cases in the present series in which the life of the patient was saved by the results of cytologic examination, for in most instances the lesion was intra-epithelial

and the complete life history of intra-epithelial cancer is not known. However, it seems reasonable to believe that by detection of unsuspected yet easily curable cancer in 80 cases, a number of lives must have been saved. Added to this obvious benefit is the peace of mind of more than 11,000 women from 17,000 "negative" reports.

To the authors, the taking of smears has become so much a part of routine examination of patients when they are observed for the first time that it would seem difficult to do without them. After four years the entire program as here outlined is more satisfactory than ever. On the other hand, any such screening program must be developed with care and caution. The potential benefit is so great that premature misuse must not be permitted to bring discredit to the method.

One valid obstacle to screening of the population in general in research centers and in cancer detection centers has been the high cost per detection. However, in the authors' experience with the screening method as adapted to use in private practice, the cost is all willingly borne by the patients, with rare exceptions. The value to any woman of a negative report seems to be equal to the small cost. Therefore, when an occasional smear is reported as

"positive" and cancer is detected, the cost per detection is the present cost of preparing and examining one slide: \$3.50.

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